HIV drug remains unproven without placebo trial

Ethical concerns over use of a placebo weaken evidence for the benefits of nevirapine.

Sir — While raising concerns about "standards of record keeping" in the HIVNET 012 trial in Uganda, in your News story "Activists and researchers rally behind AIDS drug for mothers" (*Nature* **432,** 935; 2004), you overlook a greater flaw. None of the available evidence for nevirapine comes from a trial in which it was tested against a placebo. Yet, as the study's senior author has said (see www.hopkinsmedicine.org/hmn/S01/feature.html), a placebo is the only way a scientist can assess a drug's effectiveness with scientific certainty.

The HIVNET 012 trial abandoned its placebo group in early 1998 after only 19 of the 645 mothers randomized had been treated, under pressure of complaints that the use of a placebo was unethical.

The HIV transmission rate reported for nevirapine in the HIVNET 012 study was 13.1%. However, without antiretroviral treatments, mother-to-child transmission rates of HIV vary from 12% to 48%. The HIVNET 012 outcome is higher than the 12% transmission rate reported in a prospective study of 561 African women given no antiretroviral treatment (J. Ladner *et al. J. Acquir. Immun. Def. Syndr. Hum. Retrovirol.* **18,** 293–298; 1998).

There are also reports of placebo-group transmission rates that vary within the same hospital and between hospitals, as well as during different time periods of the same study. One study reported a lower transmission rate in the placebo group than with no treatment.

On what basis can it be claimed that "there's nothing that has in any way invalidated the conclusion that single-dose nevirapine is effective for reducing mother-to-child transmission"? Without supporting evidence from a placebo-controlled randomized trial, such statements seem unwarranted.

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Concern over deep-sea reefs is widespread

Sir — As a deep-sea biologist I was surprised to read the letter by Kjartan Hoydal from the North-East Atlantic Fisheries Commission (*Nature* **433,** 105; 2005).

Contrary to Hoydal's contention that the News Feature "Sink or swim" (*Nature* **432,** 12–14; 2004) reflects a campaign by a few scientists and non-governmental organizations, the scientific evidence that fisheries are a threat to newly discovered deep-sea habitats is well documented and has been acknowledged by several governments.

The concerns raised in your News Feature are shared by many deep-sea biologists: 1,136 scientists from 69 countries signed a recent petition to the United Nations on this issue. Many governments and international bodies also believe that bottom trawling and other fishing practices are causing significant damage to deep-sea habitats.

Deep-sea coral reefs have been known for 200 years or more, but our understanding of their potential contribution to marine biodiversity is more recent, owing to new technologies that allow direct imaging of the deep-sea floor. This technology has also provided graphic evidence of destruction of these habitats by bottom trawling.

For example, it is estimated that off Norway up to 50% of reefs, formed by the coral *Lophelia pertusa*, have already been affected by fishing. In the Northern Rockall Trough, northwest of Scotland, evidence of damage to coral has been seen both in video images and in acoustic pictures of the seabed.

The United Nations Environment Programme (UNEP) recently published a report by several world experts on deep-sea coral reefs: *Cold-water Coral Reefs: Out of Sight, No Longer out of Mind* (UNEP-World Conservation Monitoring Centre Biodiversity Series No. 22), available at www.unep-wcmc.org. The report states: "Undoubtedly, the greatest and most irreversible damage is due to the increasing intensity of deep-water trawling that relies on the deployment of heavy gear which 'steamrollers' over the sea floor."

This report was endorsed by environment ministers from several European nations. Because of quantitative evidence of trawling damage, the Norwegian government has banned bottom trawling from areas in which *L. pertusa* reefs occur. Measures have also been taken to protect *L. pertusa* in the northern Rockall Trough (European Commission Regulation no. 1475/2003).

The impacts of deep-sea trawling on coral reefs have been well documented in other parts of the world, including seas off Nova Scotia, the southern United States southern Australia.

I welcome the North-East Atlantic Fisheries Commission's recent move to protect some deep-sea habitats in the North Atlantic. However, the fishing industry has little awareness of the environmental damage caused by trawling and other fishing practices.

Sustainable management of the deep-ocean environment will require a substantial and joint effort by marine scientists, fisheries managers and the fishermen themselves.

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Brown knew particles were smaller than pollen

Sir — In your Year of Physics supplement (*Nature* **433,** 213–257; 2005), several authors repeat the mistaken idea that the botanist Robert Brown observed the motion that now carries his name while watching the irregular motion of pollen grains in water. The microscopic particles involved in the characteristic jiggling dance Brown described were much smaller clay particles. I have regularly studied pollen grains in water suspension under a microscope without ever observing brownian motion.

From the title of Brown's 1828 paper "A Brief Account of Microscopical Observations … on the Particles contained in the Pollen of Plants…", it is clear that he knew he was looking at smaller particles (which he estimated at about 1/500 of an inch in diameter) than the pollen grains.

Having observed 'vivid motion' in these particles, he next wondered if they were alive, as they had come from a living plant. So he looked at particles from pollen collected from old herbarium sheets (and so presumably dead) but also found the motion. He then looked at powdered fossil plant material and finally inanimate material, which all showed similar motion.

Brown's observations convinced him that life was not necessary for the movement of these microscopic particles. Brown was not the first to observe the motion that now carries his name and that Einstein famously explained. However, he was convinced his was the first really detailed study of the phenomenon and he clearly hoped for priority for his description.

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